

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-94. (canceled)

95. (new) A method of stimulating stem cell recruitment, proliferation, or differentiation to stimulate myelopoiesis comprising,

identifying a mammalian subject in need of stem cell recruitment, proliferation, or differentiation to treat, prevent, or reduce myelosuppression, and

administering to the mammalian subject a composition comprising a vascular endothelial growth factor B (VEGF-B) product, in an amount effective to stimulate myelopoiesis in the subject.

96. (new) The method of claim 95, wherein the mammalian subject is human.

97. (new) The method of claim 95, wherein the identifying comprises selecting a subject selected from the group consisting of:

- (a) a subject undergoing antineoplastic chemotherapy;
- (b) a bone marrow transplant subject; and
- (c) a subject undergoing antineoplastic radiation therapy.

98. (new) The method of claim 97, wherein the administering comprises administering the composition contemporaneously with, or after, administering at least one of the antineoplastic chemotherapy, the bone marrow transplant, and the antineoplastic radiation therapy.

99. (new) The method of claim 95, wherein the identifying comprises:
measuring circulating white blood cells or bone-marrow derived stem cells in the subject to screen for myelosuppression.

100. (new) The method of claim 99, wherein the measuring comprises measuring at least one of CD34+ stem cells and hematopoietic stem cells.

101. (new) The method of any one of claims 95, wherein the method further comprises monitoring the number of circulating white blood cells or bone-marrow derived stem cells after administration of the composition.

102. (new) The method of claim 101, wherein the monitoring comprises detection of at least one cell surface marker selected from the group consisting of VEGFR-1, VEGFR-2, and CD34.

103. (new) The method of any one of claims 95, further comprising administering to said subject an agent selected from the group consisting of:

(a) granulocyte colony stimulating factor (G-CSF), macrophage-CSF (M-CSF), granulocyte-macrophage-CSF (GM-CSF), interleukin-3 (IL-3), stem cell factor (SCF), vascular endothelial growth factor (VEGF), vascular endothelial growth factor C (VEGF-C), vascular endothelial growth factor D (VEGF-D), platelet derived growth factor A (PDGF-A), platelet derived growth factor B (PDGF-B), platelet derived growth factor C (PDGF-C), platelet derived growth factor D (PDGF-D), and placental growth factor (PIGF);

(b) a polynucleotide comprising a nucleotide sequence encoding any member of (a), and

(c) combinations thereof.

104. (new) The method of claim 95, wherein the VEGF-B product comprises a VEGF-B polypeptide.

105. (new) The method of claim 104, wherein the VEGF-B is glycosylated.

106. (new) The method of claim 95, wherein the VEGF-B product comprises a polynucleotide that encodes a VEGF-B polypeptide.

107. (new) The method of claim 106, wherein the VEGF-B product comprises a viral vector containing the polynucleotide.

108. (new) The method of claim 107, wherein the vector comprises a replication-deficient adenoviral or adeno-associated viral vector.

109. (new) The method of claim 104, wherein the VEGF-B polypeptide comprises the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or a fragment thereof that binds VEGFR-1.

110. (new) The method of claim 104, wherein the VEGF-B polypeptide is associated as a heterodimer with a VEGF polypeptide.

111. (new) The method of claims 104, wherein the VEGF-B polypeptide binds VEGFR-1 and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide in SEQ ID NO: 1 or 3.

112. (new) The method of claim 95, wherein the VEGF-B product further comprises a pharmaceutically acceptable carrier.

113. (new) A method of stimulating stem cell proliferation or differentiation, comprising,

obtaining a biological sample from a mammalian subject, wherein said sample comprises stem cells, and

contacting the stem cells with a composition comprising a vascular endothelial growth factor B (VEGF-B) product.

114. (new) The method according to claim 113, further comprising a step of purifying and isolating the stem cells after obtaining the sample and before the contacting step.

115. (new) The method according to claim 113, further comprising a step of purifying and isolating the stem cells after the contacting step.

116. (new) The method according to claim 115, wherein the purified stem cells comprise stem cells selected from the group consisting of VEGFR-1+ stem cells, CD34+ stem cells, CD133+ stem cells, and combinations of the same.

117. (new) The method according to claims 113, wherein the contacting comprises culturing the stem cells in a culture containing the VEGF-B product.

118. (new) The method according to any one of claims 113, further comprising a step of returning the stem cells to the mammalian subject.

119. (new) The method according to any one of claims 113, further comprising a step of transplanting the cells into a different mammalian subject.

120. (new) The method of claim 118, wherein the cells are seeded into a tissue, organ, or artificial matrices ex vivo, and said tissue, organ, or artificial matrix is attached, implanted, or transplanted into the mammalian subject.

121. (new) The method of claim 119, wherein the cells are seeded into a tissue, organ, or artificial matrices ex vivo, and said tissue, organ, or artificial matrix is attached, implanted, or transplanted into the mammalian subject.

122. (new) The method according to claim 113, wherein the mammalian subject is human.

123. (new) The method according to claim 122, wherein the human subject needs antineoplastic chemotherapy, and wherein the biological sample is obtained prior to administering a dose of chemotherapy, and wherein the stem cells are returned to the human subject after the contacting and after the dose of chemotherapy.

124. (new) The method according to any one of claims 113, wherein the VEGF-B product comprises a VEGF-B polypeptide.

125. (new) The method of claim 124, wherein the VEGF-B is glycosylated.

126. (new) The method of claim 113, wherein the VEGF-B product comprises a polynucleotide that encodes a VEGF-B polypeptide.

127. (new) The method of claim 126, wherein the VEGF-B product comprises a viral vector containing the polynucleotide.

128. (new) The method of claim 127, wherein the vector comprises a replication-deficient adenoviral or adeno-associated viral vector.

129. (new) The method of claim 124, wherein the VEGF-B polypeptide comprises the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or a fragment thereof that binds VEGFR-1.

130. (new) The method of claim 124, wherein the VEGF-B polypeptide is associated as a heterodimer with a VEGF polypeptide.

131. (new) The method of claims 124, wherein the VEGF-B polypeptide binds VEGFR-1 and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide in SEQ ID NO: 1 or 3.

132. (new) The method of claim 113, wherein the VEGF-B product further comprises a pharmaceutically acceptable carrier.

133. (new) A method of stimulating stem cell recruitment, proliferation, or differentiation comprising,

identifying a mammalian subject in need of stem cell recruitment, proliferation, or differentiation to treat or prevent ischemia, and
administering to the subject a composition comprising a platelet derived growth factor (PDGF) product.

134. (new) The method of claim 133, wherein the subject is human.

135. (new) The method of claim 133, wherein the PDGF product comprises at least one member selected from the group consisting of PDGF-A, PDGF-B, PDGF-C, and PDGF-D products.

136. (new) The method of claim 133, wherein the PDGF product binds PDGFR- α .

137. (new) The method of claim 133, wherein the PDGF product comprises at least a PDGF-C product.

138. (new) The method of claim 133, wherein the PDGF product comprises a PDGF polypeptide.

139. (new) The method of claim 133, wherein the PDGF product comprises a polynucleotide that encodes a PDGF polypeptide.

140. (new) The method of claim 139, wherein the PDGF product comprises a viral vector containing the polynucleotide.

141. (new) The method of claim 140, wherein the vector comprises a replication-deficient adenoviral or adeno-associated viral vector.

142. (new) The method of claim 138, wherein the PDGF polypeptide comprises a portion of the amino acid sequence set forth in SEQ ID NO: 7 or 9 that is effective to bind PDGFR-alpha or PDGFR-beta.

143. (new) The method of claim 138, wherein the PDGF polypeptide binds PDGFR-alpha or PDGFR-beta and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide in SEQ ID NO: 6 or 8.

144. (new) The method of claim 133, wherein the PDGF polypeptide comprises a member selected from the group consisting of a PDGF-A polypeptide, a PDGF-B polypeptide, a PDGF-C polypeptide, a PDGF-D polypeptide, combinations thereof, or fragments thereof that bind to at least one of PDGF receptors alpha and beta (PDGFR-alpha, PDGFR-beta).

145. (new) The method of claims 133, wherein the PDGF polypeptide comprises a PDGF-C or PDGF-D polypeptide or a fragment thereof that binds to at least one of PDGF receptors alpha and beta (PDGFR-alpha, PDGFR-beta).

146. (new) The method of claims 133, wherein the composition further comprises a pharmaceutically acceptable carrier.

147. (new) The method of claims 133, further comprising administering to said subject an agent selected from the group consisting of:

(a) granulocyte colony stimulating factor (G-CSF), macrophage-CSF (M-CSF), granulocyte-macrophage-CSF (GM-CSF), interleukin-3 (IL-3), stem cell factor (SCF), vascular endothelial growth factor (VEGF), vascular endothelial growth factor B (VEGF-B) vascular endothelial growth factor C (VEGF-C), vascular endothelial growth factor D (VEGF-D), platelet derived growth factor A (PDGF-A), platelet derived growth factor B (PDGF-B), platelet derived growth factor C (PDGF-C), platelet derived growth factor D (PDGF-D), and placental growth factor (PIGF);

(b) a polynucleotide comprising a nucleotide sequence encoding any member of (a), and

(c) combinations thereof.

148. (new) A method of stimulating stem cell proliferation or differentiation, comprising,

obtaining a biological sample from a mammalian subject, wherein said sample comprises stem cells, and

contacting the stem cells with a composition comprising a platelet derived growth factor C (PDGF-C) product or platelet derived growth factor D (PDGF-D) product.

149. (new) The method according to claim 148, further comprising contacting the cells with at least one additional PDGF product selected from the group consisting of a PDGF-A product, a PDGF-B product, a PDGF-C product and a PDGF-D product.

150. (new) The method according to claim 148, further comprising a step of isolating the stem cells after obtaining the sample and before the contacting step.

151. (new) The method according to claim 148, further comprising a step of purifying and isolating the stem cells after the contacting step.

152. (new) The method according to claim 151, wherein the purified stem cells comprise cells that express PDGFR-alpha.

153. (new) The method according to claim 151, wherein the purified stem cells comprise CD34+ stem cells.

154. (new) The method according to claim 148, wherein the contacting comprises culturing the stem cells in a culture containing the PDGF-C product or PDGF-D product.

155. (new) The method according to claim 148, further comprising a step of returning the stem cells to the mammalian subject after the contacting step.

156. (new) The method according to claim 148, further comprising a step of transplanting the cells into a different mammalian subject after the contacting step.

157. (new) The method of claim 155, wherein the cells are seeded into a tissue, organ, or artificial matrix ex vivo, and said tissue, organ, or artificial matrix is attached, implanted, or transplanted into the mammalian subject.

158. (new) The method of claim 156, wherein the cells are seeded into a tissue, organ, or artificial matrix ex vivo, and said tissue, organ, or artificial matrix is attached, implanted, or transplanted into the mammalian subject.

159. (new) The method according to claims 148, wherein the mammalian subject is human.

160. (new) The method according to claim 159, wherein the human subject needs antineoplastic chemotherapy, and wherein the biological sample is obtained prior to administering a dose of chemotherapy, and wherein the stem cells are returned to the human subject after the contacting and after the dose of chemotherapy.

161. (new) The method of claim 148, wherein the PDGF-C product or PDGF-D product comprises a PDGF-C polypeptide or PDGF-D polypeptide.

162. (new) The method of claim 148, wherein the product comprises a polynucleotide that encodes a PDGF-C polypeptide or a PDGF-D polypeptide.

163. (new) The method of claim 162, wherein the product comprises a viral vector containing the polynucleotide.

164. (new) The method of claim 163, wherein the vector comprises a replication-deficient adenoviral or adeno-associated viral vector.

165. (new) The method of claims 161, wherein the polypeptide comprises a portion of the amino acid sequence set forth in SEQ ID NO: 7 or 9 that is effective to bind PDGFR-alpha or PDGFR-beta.

166. (new) The method of claim 161, wherein the PDGF polypeptide binds PDGFR-alpha or PDGFR-beta and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide in SEQ ID NO: 6 or 8.

167. (new) The method of claim 148, wherein the composition further comprises a pharmaceutically acceptable carrier.

168. (new) The method of claim 148, further comprising administering to said subject an agent selected from the group consisting of:

(a) granulocyte colony stimulating factor (G-CSF), macrophage-CSF (M-CSF), granulocyte-macrophage-CSF (GM-CSF), interleukin-3 (IL-3), stem cell factor (SCF),

vascular endothelial growth factor (VEGF), vascular endothelial growth factor B (VEGF-B), vascular endothelial growth factor C (VEGF-C), vascular endothelial growth factor D (VEGF-D), platelet derived growth factor A (PDGF-A), platelet derived growth factor B (PDGF-B), platelet derived growth factor C (PDGF-C), platelet derived growth factor D (PDGF-D), and placental growth factor (PlGF);

- (b) a polynucleotide comprising a nucleotide sequence encoding any member of (a), and
- (c) combinations thereof.

169. (new) The method of claim 150, wherein the isolating comprises isolating AC133+/CD34+ cells from the biological sample.

170. (new) The method according to claim 148, wherein the contacting comprises contacting the stem cells with the composition until stem cells differentiate into CD144+ cells.

171. (new) The method according to claim 148, wherein the contacting comprises contacting the stem cells with the composition until stem cells differentiate into SMA+/CD144-/CD31-/CD34- cells.

172. (new) The method according to claim 148, wherein the composition further comprises a VEGF-A product.

173. (new) The method according to claim 148, wherein the contacting comprises culturing the stem cells in a culture containing the PDGF-C product.

174. (new) The method according to claim 148, further comprising a step of returning the stem cells to the mammalian subject after the contacting step.

175. (new) The method of claim 174, wherein the cells are seeded into a tissue, organ, or artificial matrix ex vivo, and said tissue, organ, or artificial matrix is attached or implanted into the mammalian subject.

176. (new) The method according to claim 148, further comprising a step of transplanting the cells into a different mammalian subject after the contacting step.

177. (new) The method of claim 176, wherein the cells are seeded into a tissue, organ, or artificial matrix ex vivo, and said tissue, organ, or artificial matrix is attached or transplanted into the different mammalian subject.

178. (new) The method according to claim 148, wherein the mammalian subject is human.

179. (new) The method according to claim 178, wherein the human subject has an ischemic condition.

180. (new) The method of claim 161, wherein the polypeptide comprises an amino acid sequence at least 95% identical to SEQ ID NO: 7 or 9 and binds to at least one receptor selected from PDGFR-alpha and PDGFR-beta.

181. (new) The method of claim 161, wherein the polypeptide comprises an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 10 and binds to and/or activates at least one receptor selected from PDGFR- α/α and PDGFR- α/β .

182. (new) The method of claim 180, wherein the PDGF-C polypeptide binds PDGFR- α and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide in SEQ ID NO: 6.

183. (new) The method of claim 161, wherein the polypeptide binds PDGFR-alpha or PDGFR-beta and is encoded by a polynucleotide that hybridizes under stringent conditions with the complement of the polynucleotide of SEQ ID NO: 6 or 8.

184. (new) A method of stimulating stem cell proliferation or differentiation, comprising,
obtaining a biological sample from a mammalian subject,
wherein said sample comprises stem cells;
contacting a first aliquot of the stem cells with a first composition comprising a first growth factor product selected from a VEGF-B product and PDGF-C product; and
contacting a second aliquot of the stem cells with a second composition comprising a second growth factor product independently selected from the

group consisting of VEGF-A, VEGF-B, VEGF-C, VEGF-D, PDGF-A, PDGF-B, PDGF-C, and PIGF products,

wherein the first and second growth factor products are not the same.

185. (new) The method of claim 184, wherein the first growth factor product is a PDGF-C product and the second growth factor product is a VEGF-A product.

186. (new) A method of promoting differentiation of stem cells into both endothelial and smooth muscle cells, comprising:

obtaining a biological sample from a mammalian subject, wherein said sample comprises stem cells; and

contacting the cells with a composition comprising a platelet-derived growth factor-C (PDGF-C) product, in an amount and for a time sufficient to cause the cells to differentiate into both endothelial and smooth muscle cells.

187. (new) The method according to claim 184, further comprising returning the cells to the mammalian subject after the contacting.

188. (new) The method of claim 187, wherein the mammalian subject has an ischemic condition.

189. (new) A method of ameliorating an ischemic condition comprising:

- (a) diagnosing a mammalian subject with an ischemic condition;
- (b) isolating a biological sample from the mammalian subject, wherein the biological sample comprises stem cells;
- (c) contacting the cells with a composition comprising a platelet-derived growth factor-C (PDGF-C) product, in an amount and for a time sufficient to cause the cells to differentiate into both endothelial and smooth muscle cells; and
- (d) returning the cells to the mammalian subject.

190. (new) The method according to claim 189, wherein the returning comprises implanting or injecting the cells into or adjacent to ischemic tissue of the mammalian subject.

IN THE DRAWINGS

The attached 13 sheets of drawings include FIGS. 1a-8c, which replace the original 13 sheets of drawings including FIGS. 1a-8c.

Attachment: Replacement sheets (13);